A STUDY OF THE MECHANISMS OF THE THERMAL AND BASE INDUCED CONVERSIONS OF N-NITROSO-N-ALKYLAMINE DERIVATIVES TO DIAZOALKANES

By
DARREL LEE MUCK

A DISSERTATION PRESENTED TO THE GRADUATE COUNCIL OF
THE UNIVERSITY OF FLORIDA
IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE
DEGREE OF DOCTOR OF PHILOSOPHY

UNIVERSITY OF FLORIDA
August, 1965

ACKNOWLEDGMENTS

The author wishes to express his appreciation to his major professor, Dr. W. M. Jones, for the professional inspiration and personal assistance without which this work could not have been accomplished.

Special thanks must also be tendered to his wife, Judy, who has gracefully endured considerable harassment during the period of this work.

The National Science Foundation is also to be acknowledged for providing financial assistance.

TABLE OF CONTENTS

		Page
[illegible]		ii
LIST OF TABLES		iv
Chapter		
I.	THE MECHANISM OF THE THERMAL CONVERSION OF N-NITROSO-N-(2,2-DIPHENYLCYCLOPROPYL)UREA TO 2,2-DIPHENYLDIAZOCYCLOPROPANE	1
	Introduction	1
	Results and Discussion	5
II.	THE MECHANISM OF THE LITHIUM METHOXIDE INDUCED CONVERSION OF N-NITROSO-N-(2,2-DIPHENYLCYCLOPROPYL)UREA TO 2,2-DIPHENYLDIAZOCYCLOPROPANE.	10
	Introduction	10
	Results and Discussion	15
III.	GENERALIZATION OF THE MECHANISM OF THE ALKOXIDE INDUCED CONVERSION OF VARIOUS N-NITROSO-N-ALKYLAMINE DERIVATIVES TO DIAZOALKANES.	26
	Introduction	26
	Results	30
	Discussion	30
IV.	EXPERIMENTAL	42
V.	SUMMARY	74
LIST OF REFERENCES		76
BIOGRAPHICAL SKETCH		79

LIST OF TABLES

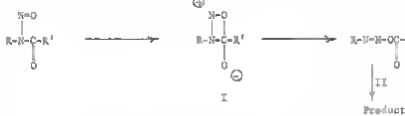
Table		Page
1.	Decomposition of N-Nitroso-N-Alkylureas . .	31
2.	Decomposition of N-Nitroso-N-Alkylurethans. . .	32
3.	Decomposition of N-Nitroso-N-Alkylamides . . .	33
4.	Conditions for Producing Phenyldiazomethane . .	34

CHAPTER I

THE MECHANISM OF THE THERMAL CONVERSION OF N-NITROSO-N-(2,2-DIPHENYLCYCLOPROPYL)UREA TO 2,2-DIPHENYLDIAZOCYCLOPROPANE

Introduction

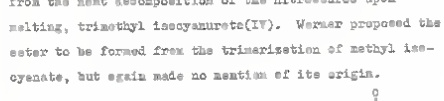
The mechanism of the thermal decomposition of N-nitrosoamides has been carefully examined and there seems to be little doubt but that the reaction proceeds by initial rearrangement (probably through intermediate I) to give the diazoester II which then loses nitrogen to give the observed products.[1]



On the other hand, the thermal decomposition of N-nitroso-N-alkyl(or aryl)ureas has received relatively little attention. In fact, only two systems are known to have been studied. The first, N-nitroso-N-methylurea, was investigated in 1919 by Werner[2] who studied the decomposition in refluxing ethyl alcohol. The major product observed by Werner was ethyl allophanate(III), which he postulated was formed from the reaction of isocyanic acid and ethanol.

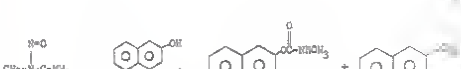
III

Werner did not attempt to explain the origin of the isocyanic acid. He then proceeded by identifying the product from the neat decomposition of the nitrosoures upon melting, trimethyl isocyanurate(IV). Werner proposed the ester to be formed from the trimerization of methyl isocyanate, but again made no mention of its origin.



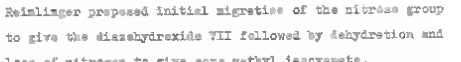
IV

Later, in 1956, Huisgen and Reimlinger investigated the thermal decomposition of N-nitroso-N-methylurea in benzene.[16] Under these conditions, the trimethyl isocyanurate(IV) was isolated in 30 per cent yield. The origin of this ester was again presumed to be from the trimerization of methyl isocyanate. Evidence in support of the intermediacy of CH_3-N=C=O was obtained by effecting the decomposition in the presence of β-naphthol. From this set of conditions was obtained 13.7 per cent of the expected urethan V plus 23.5 per cent of β-naphthyl methyl ether VI.



V VI

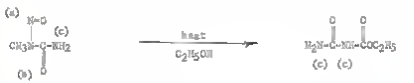
As a reasonable explanation for these results, Huisgen and Reimlinger proposed initial migration of the nitroso group to give the diazohydroxide VII followed by dehydration and loss of nitrogen to give some methyl isocyanate.



VII

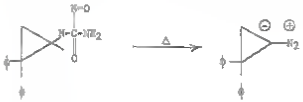
However, some four years later, Clusius and Endtinger[3] reported a thorough investigation of this same reaction employing tagged nitrogen and made the rather surprising observation that the $-NH_2$ nitrogen(c) of the nitrosourea appeared in the trimethyl isocyanurate rather than the nitrogen to which the nitroso was attached (as would be expected by the Huisgen and Reimlinger mechanism).

Clusius and Endtinger also studied the decomposition in ethyl alcohol, and isolated the ethyl allophanate(III) as reported earlier by Werner. Again using tagged nitrogen, the $-NH_2$ nitrogen of the nitrosourea was observed to be present in both positions of the allophanate ester.



Clusius and Endtinger were not able to justify either of these results and concluded their paper with the statement that "a convincing formulation for the reaction mechanism is not yet possible."

Shortly after these reports, a study of the thermal decomposition of N-nitroso-N-(2,2-diphenylcyclopropyl)urea (VIII) was reported by Jones, Grassley and Baarda,[4] and it was reported that only the products that would result from initial formation of 2,2-diphenyldiazocyclopropane(IX) were found, with no 2,2-diphenylcyclopropyl isocyanate being detected.

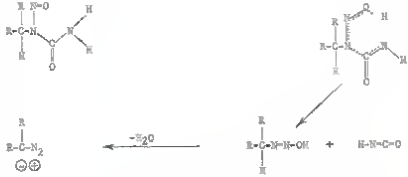


VIII IX

The purpose of this work is to propose a mechanism for these reactions that is consistent with all of the above observations and to present some additional observations that support this mechanism.

Results and Discussion

The proposed mechanism is outlined in Scheme 1. The proton transfer and expulsion of isocyanic acid may be either stepwise or concerted. It is arbitrarily pictured as a concerted reaction.

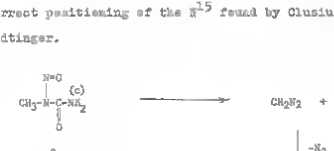


Scheme 1

Application of this mechanism to Huisgen and Reimlinger's system gives as the initial products diazomethane and isocyanic acid instead of methyl isocyanate. However, it was found here that diazomethane reacts quite rapidly with isocyanic acid to give methyl isocyanate.

$$CH_2N_2 + H\text{-}N{=}C{=}O \longrightarrow CH_3\text{-}N{=}C{=}O$$

Trimerization of methyl isocyanate from this [illegible] would lead to isocyanuric acid trimethyl ester with the correct positioning of the N^{15} found by Clusius and Endtinger.



However, when an attempt was made to effect this trimerization under Huisgen and Reimlinger's reaction conditions, negligible amounts of the trimer were obtained. Methyl isocyanate is known to polymerize to the trimer IV during attempted distillation,[5] so apparently the reaction is greatly reduced when the monomer is diluted with a solvent such as benzene. This information sheds doubt on the possibility of methyl isocyanate being the precursor to the cyanurate ester under Huisgen and Reimlinger's conditions, but does not eliminate it from consideration under the conditions used by Werner.

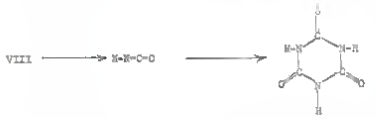
A more feasible explanation of the observations of Huisgen and Reimlinger as well as Clusius and Endtinger would involve initial trimerization of isocyanic acid[6] to cyanuric acid followed by reaction with diazomethane to give the trimethyl ester. This possibility was confirmed by treating cyanuric acid with diazomethane. Reaction was not as rapid as with isocyanic acid but the reaction did proceed at a reasonable rate at 0° to give the predicted product.

The proposed mechanism also explains the observation of Huisgen and Reimlinger that 23.5 per cent of methyl beta-naphthyl ether (VI) is also formed in their reaction.

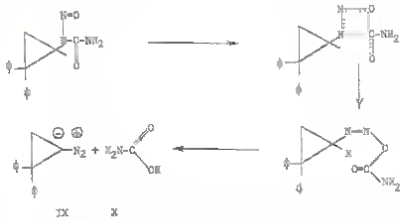
Application of this same scheme to the N-nitroso-N-(2,2-diphenylcyclopropyl)urea system (VIII) readily explains the observed products resulting from decomposition of 2,2-diphenyldiazocyclopropane (IX).

Further evidence for the proposed scheme arises from a more careful examination of the products arising from the decomposition of the nitrosocyclopropyl urea VIII. Thus, in addition to the decomposition products of 2,2-diphenyldiazocyclopropane, there was invariably noted a white insoluble solid. Much of this was found in the condenser above the reaction flask. Examination of this solid showed that it was cyanuric acid (isolated in 82% yield). The formation of this non-volatile material in the condenser

left no doubt but that it arose from the [illegible] merization of isocyanic acid.[6]



One possible alternate reaction route that could not a priori be excluded involves a rearrangement analogous to that believed to occur in the thermal decomposition of N-nitrosoamides.



However, in order for this mechanism to explain the various observations, carbamic acid (X) must dehydrate under the reaction conditions to give isocyanic acid.

X

This possibility was tested by treating lithium and sodium carbamate with p-toluenesulfonic acid in refluxing benzene. The only products were ammonium p-toluenesulfonate and the alkali metal p-toluenesulfonates. This, carbamic acid apparently decomposes in the normal fashion[7] in refluxing benzene to give carbon dioxide and ammonia.

Another bit of pertinent data was obtained when the corresponding dimethylamide derivative, N-nitroso-N-(2,2-diphenylcyclopropyl)N',N'-dimethylurea[8] was found not to evolve nitrogen when heated under normal reaction conditions. When this compound was heated more strongly, it was slowly transformed into unknown products without gas evolution. Examination of this crude decomposition product revealed none of the normal diazocyclopropane decomposition product, diphenylallene.

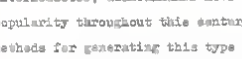
Finally, the similarity between the mechanism proposed in Scheme 1 and the mechanism which is believed to obtain in the alkoxide induced conversion of N-nitroso-N-cyclopropylureas to diazocyclopropanes should be pointed out. It is believed that the reaction proceeds by initial attack of alkoxide on the nitroso nitrogen followed by proton transfer, loss of isocyanic acid and loss of base. This is outlined in Chapter II.

CHAPTER II

THE MECHANISM OF THE LITHIUM ETHOXIDE INDUCED CONVERSION OF N-NITROSO-N-(2,2-DIPHENYLCYCLOPROPYL)UREA TO 2,2-DIPHENYLDIAZOCYCLOPROPANE

Introduction

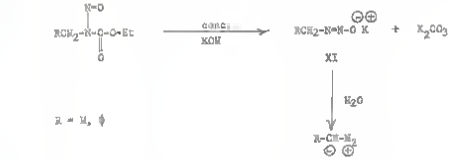
Because of their usefulness as organic reaction intermediates, diazoalkanes have enjoyed considerable popularity throughout this century. One of the more common methods for generating this type of intermediate involves reaction of nitrosoalkylamine derivatives with base. This general type of reaction was discovered in 1895 by von Pechmann,[9] when he prepared phenyldiazomethane from the potassium hydroxide induced decomposition of N-nitroso-N-benzylurethan.



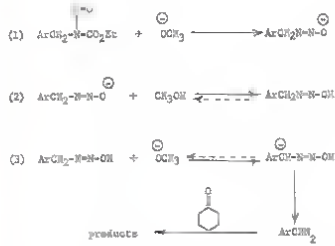
Van Pechmann's pioneering work in this area has since been expanded by many investigators to include the preparation of diazoalkanes from N-nitroso-N-alkylamides and N-nitroso-N-alkylureas.

The mechanism of these conversions has also been a subject of some interest since the early part of this

century. As early as 1902, Hantzsch and Lehmann[10] were able to isolate the potassium salts of methyl and benzyl diazohydroxide (XI) (named as potassium alkyldiazotates) from the reaction of concentrated potassium hydroxide with N-nitroso-N-alkylurethans, and reported that they react with water to give the corresponding diazoalkanes. The obvious conclusion that was drawn from these results was that the base had attacked the carbonyl carbon atom,



This conclusion apparently set a precedent for the mechanism of the base induced decomposition of nitrosoalkylamine derivatives, as has been evidenced by its application to the base induced decomposition of other nitrosoalkylurethans, nitrosoamides and nitrosoureas.[11,12] For example, in 1955, Gutsche and Johnson[13] reported a rather thorough study of the methoxide induced decomposition of a series of substituted benzyl nitrosourethanes.



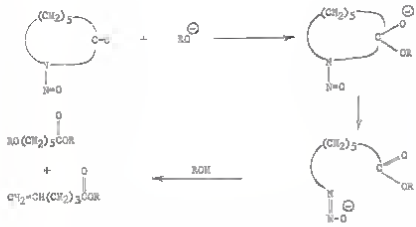
By suggesting the formation of methyl ethyl carbonate in the first step here, the authors obviously implied that the methoxide ion had attacked the carbonyl carbon atom in a manner analogous to the Hantzsch and Lehmann mechanism.

An application of this mechanism to the base induced decomposition of nitrosoureas was presented in 1960 by Applequist and McGrear,[14] when they prepared diazocyclobutane from the ethoxide induced decomposition of N-nitroso-N-cyclobutylurea. Again, attack of base on the carbonyl carbon atom was implied by their suggestion that ethyl carbazate was one of the products, although again its presence was not actually demonstrated.

Scheme 2

As a matter of fact, the literature shows only two cases where the isolated products definitely implicate attack of the base on the carbonyl carbon atom. In one instance, Bollinger, Hayes and Siegel[15] reported that isolation of 67 per cent methyl ethyl carbonate from the methoxide induced decomposition of N-nitroso-N-cyclohexylurethane in methanol.

In a second case, Huisgen and Reimertshofer[11] effected the reaction of methoxide in methanol with a cyclic N-nitroso-amide derivative, nitrosocaprolactam, and isolated methyl ester products, again strongly suggesting attack of methoxide on the carbonyl carbon.



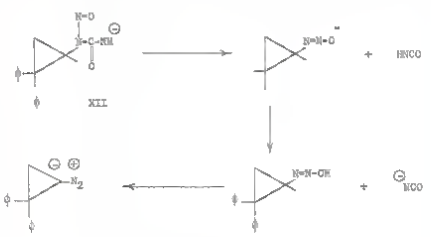
Recently, a study was made of the formation of a diazocyclopropane by the ethoxide induced decomposition of N-nitroso-N-(2,2-diphenylcyclopropyl)urea in non-polar solvents.[8] In the course of the study, it was determined that the initial step in the reaction did not involve attack of the base on the carbonyl carbon atom. This was accomplished by showing that the product expected from attack at the carbonyl position, ethyl carbonate, was not formed in the reaction. It was also shown that the corresponding diazotate salt was stable to reaction conditions.

The purpose of this study was to further investigate the mechanism of the ethoxide induced decomposition of N-nitroso-N-(2,2-diphenylcyclopropyl)urea in non-polar solvents.

Results and Discussion

There are at least two other points on the nitroso-[illegible] besides the carbonyl group where attack of the base could occur. These are the $-NH_2$ and the nitroso group. Attack at each of these points will be considered separately.

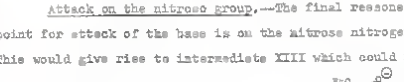
Attack on the $-NH_2$.--Attack of the base on the $-NH_2$ group would most likely proceed by simple proton abstraction to give anion XII.[16] The one reasonable route that this anion could follow to the diazocyclopropane would be by loss of isocyanic acid to give the diazotate, followed by an acid-base reaction of the diazotate with isocyanic acid to give cyanate ion and the diazohydroxide, an intermediate that could react further to give the diazocyclopropane.



Scheme 3

[illegible] stereochemistry since lithium cyanate is a [illegible] of the reaction.* However, the scheme was [illegible] by the finding that under reaction conditions, the diazotate is stable to isocyanic acid.

Attack on the nitroso group.--The final reasonable point for attack of the base is on the nitroso nitrogen. This would give rise to intermediate XIII which could react



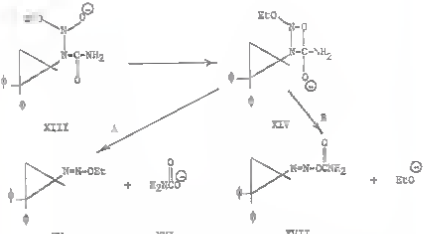
XIII

further by either of two paths.

In the first path, the negative oxygen could attack the carbonyl carbon to give the cyclic intermediate XIV which could then collapse according to Scheme 4 to give either the diazoether XV and lithium carbamate (XVI), or the diazourethan XVII.

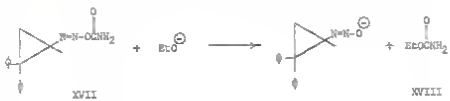
---

* As the result of a study made in 1919, Werner[2] reported that sodium cyanate was isolated from the sodium ethoxide induced decomposition of N-nitroso-N-methylurea. Werner simply determined the stoichiometry of the reaction and did not attempt to determine the origin of the cyanate. In addition to sodium ethoxide, Werner examined ammonia as a base for inducing decomposition of the nitrosourea and found ammonium cyanate to be a product of this reaction. As before, there was no mention made of a possible origin of the cyanate.

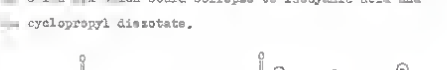


Scheme 4

The former of these possibilities (Path A) was excluded by independently showing that lithium carbamate does not decompose to lithium cyanate (the observed reaction product) under the conditions of the reaction. Decomposition of the diazourethan XVII to the diazocyclopropane could proceed by any of three routes. In the first, XVII could react with base to give ethyl carbamate and the cyclopropyl diazotate. This possibility has already been excluded by the stability of the diazotate and the absence of XVIII.

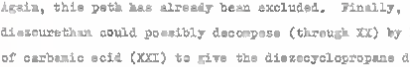


In the second path, it could [illegible] which could collapse to isocyanic acid and the cyclopropyl diazotate.



XIX

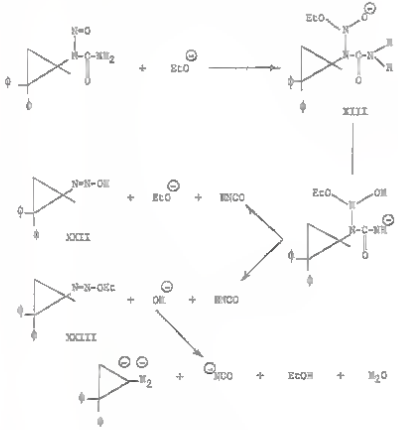
Again, this path has already been excluded. Finally, the diazourethan could possibly decompose (through XX) by loss of carbamic acid (XXI) to give the diazocyclopropane directly.



XX XXI

However, to explain the observed lithium cyanate product, this mechanism would require either decomposition of lithium carbamate to lithium cyanate or carbamic acid to isocyanic acid. Both of these possibilities were excluded, the former as described above and the latter by treating lithium and sodium carbamate with p-toluenesulfonic acid under the conditions of the reaction and showing that the only products observed were those expected,[7] ammonia and carbon dioxide.

The [illegible] group of [illegible]oh the negative oxygen of intermediate XIII might be expected to attack is the $-NH_2$ group. Proton abstraction by the negative oxygen of anion XIII followed by (or concomitant with) collapse of the resultant anion and loss of ethoxide or hydroxide could give isocyanic acid plus the diazohydroxide (XXII) or the diazoether (XXIII).

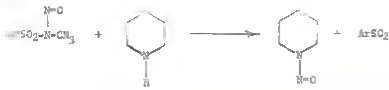


Scheme 5

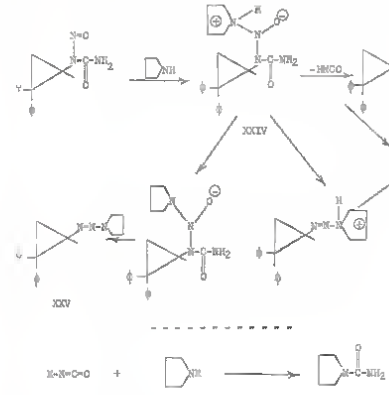
[illegible] the diazohydroxide or the diazoether could then correspond to the observed diazocyclopropane.[17] These conversions could be assisted by isocyanic acid or, possibly, induced by base as was suggested by Gutsche as well as Applequist and McGreer for the last steps of their mechanisms.

Although there was no success in obtaining direct evidence for this mechanism, it appears attractive for several reasons. In the first place, reaction of the base with the nitroso nitrogen is not without precedent. For example, Hellinger, Hayes and Siegel[15,16] found that two of the products from the reaction of N-nitroso-N-cyclohexylurethan with potassium carbonate in methanol were methyl nitrite and N-cyclohexylurethan. These products obviously arose from attack of methoxide on the nitroso nitrogen.

Similarly, Hacker and de Boer[19] found that treatment of N-methyl-N-nitroso-p-toluenesulfonamide with piperidine gave only nitrosopiperidine and N-methyl-p-toluenesulfonamide. Again, attack of base on the nitroso nitrogen was apparently involved.



A second reason which makes this mechanism appear attractive resides in the nature of the products that result from reaction of the nitrosoureas with pyrrolidine.[8] A logical extrapolation of the ethoxide mechanism to the reaction with pyrrolidine is outlined in Scheme 6.



Scheme 6

From this scheme it will be noted that the [illegible] would lead to three principal products, 2,2-diphenyl[illegible]propane, N-pyrrolidylcarboxamide (XXVI), and the [illegible] XXV. When this reaction was run in pentane at 0°, all three of these products were observed. The diazocyclopropane (ca. 80%) was detected in the usual manner. The amide was formed in essentially quantitative yield, while the triazine was formed in up to 19 per cent yield. Of these products, only the triazine sheds any real light on the mechanism of the reaction under consideration. The only two obvious sources for this material are from attack of the pyrrolidine on the nitrose nitrogen atom or by reaction of the diazocyclopropane with pyrrolidine. The latter was earlier excluded by generating the diazocyclopropane from a different source (pyrolysis of pyrrolidinium 2,2-diphenylcyclopropyldiazotate) in the presence of pyrrolidine.[8] None of the triazine was formed. Perhaps it should be pointed out that although formation of the amide XXVI suggests formation of isocyanic acid (which was independently shown to react with pyrrolidine to give a quantitative yield of the amide) it could also be explained by attack of the pyrrolidine on the carbonyl carbon.

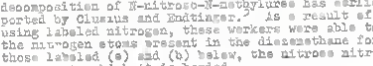
A third factor that makes this mechanism intuitively attractive is the finding that the thermal decomposition of nitrosoureas apparently also proceeds by a similar mechanism, which was pictured in Scheme 1.

The fourth factor to consider here is the observation that nitrosourea also reacts with lithium hydroxide to give almost 80 per cent of the calculated nitrogen and a mixture of lithium 2,2-diphenylcyclopropyldiazotate and 1,1-diphenylallene.* In view of the stability of the stability of the diazotate to the reaction conditions and the formation of 74 per cent lithium cyanate, the 80 per cent nitrogen most certainly arose from attack of the hydroxide on the nitroso nitrogen.** Collapse of the

---

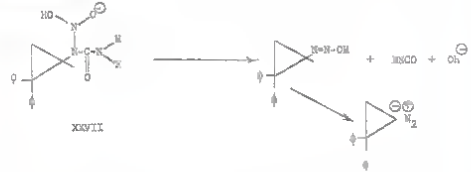
*Lithium 2,2-diphenylcyclopropyldiazotate is almost invariably found in varying small amounts in the reaction of the nitrosoureas with both lithium ethoxide and lithium hydroxide. However, there are a variety of routes by which this could arise and therefore its formation cannot be taken as strong evidence for any mechanism.

**Some information concerning the hydroxide induced decomposition of N-nitroso-N-methylurea has earlier been reported by Clusius and Endtinger.[7] As a result of a study using labeled nitrogen, these workers were able to show that the nitrogen atoms present in the diazomethane formed were those labeled (a) and (b) below, the nitroso nitrogen and the nitrogen to which it is bonded.



Although Clusius and Endtinger did not examine the remaining products of this reaction, it follows that the nitrogen present in the sodium cyanate produced would have to be that

[redacted] intermediate XXVII would give rise to the diazo-[redacted] etc, which therefore must be considered to be a



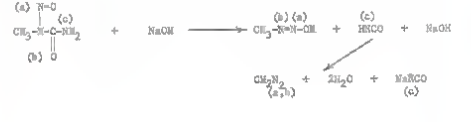
XXVII

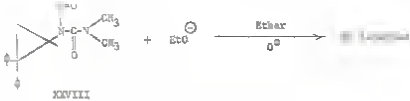
reasonable precursor to the diazocyclopropane.

Finally, it has been shown that N-nitroso-N-(2,2-diphenylcyclopropyl)-N',N'-dimethylurea XXVIII[5] is extremely unreactive with lithium ethoxide, being recovered unchanged after 24 hours under typical reaction conditions.

---

labeled (c) above. These results can readily be accommodated by the mechanism proposed here.





XXVIII

Although this single observation does not require the suggested mechanism (scheme 5), it is certainly consistent with the scheme involving proton abstraction from the -NH$_2$

CHAPTER III

GENERALIZATION OF THE MECHANISM OF THE ALKOXIDE INDUCED CONVERSION OF VARIOUS N-NITROSO-ALKYLAMINE DERIVATIVES TO DIAZOALKANES

Introduction

In Chapter II of this paper, a mechanism for the ethoxide induced decomposition of N-nitroso-N-(2,2-diphenylcyclopropyl)urea in ether was postulated (Scheme 5), and shown to be consistent with a variety of experimental results. These results were in direct conflict with conclusions previously reported by Applequist and McGreer[14] concerning the alkoxide induced decomposition of N-nitroso-N-cyclobutylurea (Scheme 2). The reaction scheme shown by these workers was apparently taken from the classical scheme for the base decomposition of nitrosourethans and nitrosoamides. The apparent difference in the path of reaction of alkoxide with the nitrosocyclopropylurea and that accepted for the same reaction of nitrosourethane and amides prompted a systematic study of the reaction of nitrosoalkylamine derivatives with base to determine what factors control the course of the reaction. The results of this study are given and discussed in the following section.

From Table 1, it is apparent that the mechanism of the first step of reaction of alkoxide with N-nitroso-N-alkylurea is independent of the alkyl group, the solvent or the particular base employed. In none of the cases was any product resulting from attack of the base on the carbonyl carbon atom observed.

The results of Table 2 indicate that the point of attack by base on N-nitroso-N-alkylurethans is not limited to one position as it was with the nitrosoureas. The amount of attack on the carbonyl carbon atom varies from about 10 per cent (with all alkyl derivatives when reacted with lithium ethoxide in aprotic solvents) to 90 per cent with the cyclohexyl derivative (decomposition by potassium carbonate in ethanol). The fact that attack at the carbonyl carbon atom is generally much less pronounced in aprotic solvents than in protic solvents should be noted. These results are consistent with those reported by Bollinger, Hayes and Siegel[15] for the reaction of N-nitroso-N-cyclohexylurethan with potassium carbonate in methanol, as well as the mechanism suggested by Gutsche and Johnson[13] for the decomposition of N-nitroso-N-benzylurethans by potassium carbonate in methanol. Finally, it should be noted that the relative amount of attack of ethoxide on the carbonyl carbon atom of nitrosourethans is apparently affected to some extent by the cation present in the base.

Table 3 summarizes the results of an investigation of the reaction of N-nitroso-N-alkylamides with base, and shows one notable result. The mode of attack on these systems is strongly influenced by the type of group attached to the carbonyl carbon atom. Thus, the benzamides showed about 50 per cent attack at the carbonyl carbon atom, while the acetamides showed 80-90 per cent attack at this position. The effect of changes in solvent, alkyl group and the cation of the base were similar to those observed in reactions of the nitrosourethans with base.

In an attempt to find optimum conditions for the synthesis of diazoalkanes from various derivatives of N-nitroso-N-alkylamines, an investigation of the normal variables involved in these base decompositions was conducted. The results of this work are shown in Table 4. Derivatives of N-nitroso-N-benzylamine were chosen for this study primarily because the diazocompound formed, phenyldiazomethane, is a stable compound. Also this type of nitroso derivative has previously been observed to lose a molecule of nitrogen and form the carbonium ion products to some extent under these conditions. It was therefore very convenient to monitor the reactions in a manner similar to that previously used by Gutsche and Johnson[13] by observing nitrogen evolution in an initial phase of the reaction (to determine the amount of carbonium ion formed) followed by

acidification of the reaction solution with acetic acid to determine (again by evolution of nitrogen) the amount of phenyldiazoacetate formed. It should be noted that the yields of diazoalkane produced in ethanol are essentially independent of the particular nitrosoamine derivative decomposed. In other words, nitrosoureas, urethans and amides are all about equivalent in the production of the diazoalkane. That the type of solvent employed had an effect on the yield of diazoalkane produced was shown when hexane was observed to be somewhat poorer than ethanol or ether, especially with the nitrosoureas. The most dramatic changes in the yield of diazoalkane produced were observed as a result of changes in the temperature and the amount of base employed. For example, the yield increased from about 55 per cent at 0° to 65 per cent at minus 20°, and to 71 per cent at minus 40°. However, at minus 40° the reaction is very sluggish. The number of moles of base also had an appreciable effect on the yield of the diazoalkane, the greater the amount of base, the better the yield.

The optimum conditions for obtaining diazoalkanes in the best yields will apparently depend on the alkyl system employed. If a stable diazotate salt is expected (as with 2,2-diphenylcyclopropyl derivatives), production of the diazotate should be minimized by decomposing the nitrosourea derivative in ether with lithium ethoxide

reaction times of the nitrosoamides and the nitrosourethans in ether are very long under these conditions). If, however, a stable diazoalkane is expected (such as phenyldiazoethane), any of the N-nitroso-N-benzylamine derivatives studied could be decomposed in ethanol at minus 20°, using an excess of lithium ethoxide. Admittedly, the yields of diazo produced were better at minus 40°, but a significant increase in reaction time creates an objection to the lower temperature.

Results

A summary of the results obtained from the investigation of factors that control the mode of reaction of alkoxide with N-nitroso-N-alkylamines is given in Tables 1, 2, 3, and 4.

Discussion

The results shown in the previous section reveal certain generalities that are particularly significant. In the reactions where ethoxide in ethanol was employed, the yield of the by-product that arises from attack of the base on the carbonyl carbon atom (e.g. diethyl carbonate from the urethane, ethyl acetate from the acetamides, etc.) varies with the nature of the group that is bonded to the carbonyl carbon. However, despite this variation in the

TABLE I[a]

DECOMPOSITION OF N-NITROSO-N-ALKYLUREAS

Entry	R-N(NO)-C(=O)-NH$_2$	Solvent	Base	Total Gas Evolution	Lithium Cyanate	Ethyl Carbamate
1	R = [b]	Et_2O	LiOEt	71	69	2
2	"	EtOH	LiOEt	92	87	2
3	"	EtOH	K_2CO_3	94	--	2
4	R =	Et_2O	LiOEt	75	76	2
5	"	EtOH	LiOEt	96	91	2
6	"	EtOH	K_2CO_3	95	--	2
7	R =	Et_2O[c]	LiOEt	78	65	2
8	R =	Et_2O	LiOEt	100	88	2
9	"	EtOH	LiOEt	100	86	2
10	"	EtOH	K_2CO_3	96	--	2
11	R = ϕCH_2[a]	Et_2O	LiOEt	100[d]	92	2
12	"	EtOH	LiOEt	97	83	2
13	"	EtOH	K_2CO_3	98	--	2

[a]The LiOEt was dissolved in 2 ml. of ethanol before addition so that the reaction conditions would be identical to those employed by Applequist and McGreer.[16]

[b]The formation of diazocyclopropane was substantiated by effecting the reaction in diethyl fumarate and isolating the pyrazoline (as its N-benzoyl derivative).

[c]The presence of phenyldiazomethane was shown by the isolation of benzoxybenzoin from its reaction with benzaldehyde.

[d]Represents the total of amounts of gas evolved in the initial step and that from decomposition of the diazo with acetic acid.

[e]All reactions were run at 0°.

TABLE 2[a]

DECOMPOSITION OF N-NITROSO-N-ALKYLURETHANS

Entry	R-N(NO)-C(=O)-OEt	Solvent	Base	Total Gas Evolution	Diethyl Carbonate
1	R = [b]	Et_2O	LiOEt	97	7
2	"	EtOH	LiOEt	52	46
3	"	EtOH	K_2CO_3	31	72
4	R = [c]	Et_2O	LiOEt	100	9
5	"	EtOH	LiOEt	100	44
6	"	EtOH	K_2CO_3	98	90
7	"	EtOH	NaOEt	100	70
8	"	EtOH	KOEt	100	78
9	R = ϕCH_2 [d]	Et_2O	LiOEt	100[e]	10
10	"	EtOH	LiOEt	100[e]	47
11	"	EtOH	K_2CO_3	100[e]	52
12	"	$MeOCH_2CH_2OMe$	LiOEt	100[e]	8
13	"	$CH_3\overset{O}{\overset{\|}{C}}CH_3$	LiOEt	100[e]	14
14	"	$CH_3\overset{O}{\overset{\|}{C}}CH_3$	LiOEt	100[e]	8
15	"	$CH_3\overset{O}{\overset{\|}{C}}CH_3$	K_2CO_3	0	N.R.

[a] All reactions were run at 25°. Analytical results accurate to ± 3%.

[b] The formation of 2,2-diphenyldimethylcyclopropane is assumed due to the fact that 1,1-diphenylallene was isolated from the reaction products.

[c] The presence of dimethylcyclohexane was shown by running the reaction in diethyl fumarate and isolating the pyrazolium (as its benzoyl derivative).

[d] Phenyldiazomethane was shown to be present by reacting it with benzaldehyde and isolating benzophenone.

[e] Represents the total of amounts of gas evolved in the initial step and that from decomposition of the diazo with acetic acid

TABLE 3[a]

DECOMPOSITION OF N-NITROSO-N-ALKYLAMIDES

Entry	R=O R-N-C-R' NO	Solvent	Base	Gas Evolved Step 1	Gas Evolved Step 2	Ethyl[b] Carboxylate	Alkali[c] Carboxylate	Benzyl Ethyl Ether
1	R = R' = ϕ[d]	Et2O	LiOEt	96	-	4	80	-
2	R = " R' = "	EtOH	LiOEt	58	-	48	40	-
3	R = " R' = "	EtOH	K_2CO_3	47	-	56	37	-
4	R = ϕCH_2 R' = ϕ[e]	Et_2O	LiOEt	48	52	5	74	[illegible]
5	R = " R' = "	EtOH	LiOEt	50	50	44	52	15
6	R = " R' = "	EtOH	K_2CO_3	50	50	54	43	50
7	R = " R' = CH_3	Et_2O	LiOEt	50	50	7	86	8
8	R = " R' = "	EtOH	LiOEt	46	54	73	23	49
9	R = " R' = "	EtOH	K_2CO_3	47	53	83	9	49

[a]Reactions were run at 25°.

[b]Respective product resulting from ethoxide attack on the carbonyl carbon atom

[c]Respective product resulting from ethoxide attack on the nitrose nitrogen atom

[d]For the preparation of this compound, see the Ph D. Dissertation of Thomas R. Tandy Jr University of Florida Dec. 1964.

[e]Phenyldiazomethane was shown to be formed by its reaction with benzaldehyde to form deoxybenzoin.

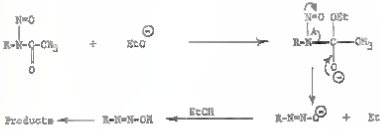
TABLE 4

CONDITIONS FOR PRODUCING PHENYLDIAZOMETHANE

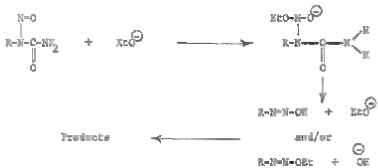
| Entry | $\overset{N=O}{\overset{|}{CH_2}}\!\!-\!\!\overset{}{N}\!\!-\!\!\overset{}{C}\!\!-\!\!R$
 $\quad\quad\quad

yield of by-product, the yield and nature of the products arising from the alkylamine portion of the various starting materials appears to be virtually independent of the amount of reaction that proceeds by attack of the base on the carbonyl carbon atom (with the exception of the one cyclopropyl system studied). They also appear to be unaffected by the nature of the group that is attached to the carbonyl carbon atom. These results suggest that there are two potentially competitive initial steps that can lead to structurally identical or similar intermediates.

In the case of the decomposition of N-nitroso-N-alkylacetamides in ethanol, the classical scheme that involves attack of the ethoxide on the carbonyl carbon atom to give the acetate ester and the alkali diazotate is probably valid.



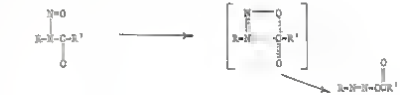
With the decomposition of N-nitroso-N-alkylureas (in any solvent), there appears to be exclusive attack of the base on the nitroso nitrogen atom in a manner analogous to that postulated for the base induced conversion of N-nitroso-N-(2,2-diphenylcyclopropyl)urea to 2,2-diphenyldiazocyclopropane.



In the case of the N-nitroso-N-alkylurethans and benzamides, there is apparently competitive attack of the base on the carbonyl carbon atom (as with the nitroso-acetanilides) to give the alkali diazotate and diethyl carbonate or ethyl benzoate along with attack on the nitroso nitrogen atom in a manner analogous to the mechanism postulated for reaction of N-nitroso-N-alkylureas with ethoxide. Obviously, however, the second stage of reaction of the latter case must follow a different path from that proposed for the nitrosoureas (no terminal N-H proton available in this case). A reasonable reaction scheme can be derived

from that given for the thermal conversion of nitroso-amides to diazoalkanes,[1] which presumably involves initial rearrangement to the corresponding diazoester.

Thermal.--

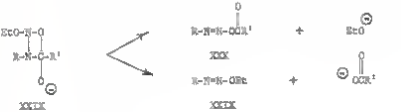


Alkoxide Induced.--

XXIX

R = ϕ, OEt

Collapse of this intermediate could proceed by two different routes, one leading to the diazoester XXX plus ethoxide and the other giving the diazoether XXXI plus a carboxylate anion.



XXIX XXX XXXI

Of these two possibilities, the latter is favored for two reasons. First, the carboxylate would be expected to be more readily displaced than the ethoxide. The second reason resides in the fact that the composition of products resulting from the alkylamine portion of the nitroso derivatives is independent of the amount of reaction that goes by attack of the base on the carbonyl carbon atom (cf. entries 9 and 10 in Table 2, and entries 12 and 15 in Table 4) as well as the group (see Table 4) that is attached to the carbonyl carbon atom. The former result (independence of products of position of base attack) suggests formation of an intermediate from attack on the nitroso nitrogen atom that is structurally similar to the likely intermediate from attack of the base on the carbonyl carbon atom, namely, the diazohydroxide. The latter result (independence of products from group attached to the carbonyl carbon atom) suggests that the group bonded to the carbonyl carbon atom is lost prior to the product forming step(s). Both of these criteria are reasonably well satisfied by postulating collapse of XXIX to give the diazoether, rather than the diazoester.

Further evidence which supports the suggested dual mechanism for the initial phase of the reaction of ethoxide with the nitrosourethanes and nitrosoamides resides in the relative amounts of attack of the base on the carbonyl

carbon and the nitroso nitrogen atoms with a variation in the nature of the group attached to the carbonyl carbon. Since a change in the group at that point should have a more severe effect on the reactivity of the carbonyl than the nitroso group, it would be expected that attack at the carbonyl carbon would decrease (relative to attack at the nitroso) as the attached group is changed from methyl to phenyl (or ethoxy) to $-NH_2$. The experimental evidence most certainly supports this prediction.

It was earlier pointed out that the 2,2-diphenylcyclopropyl system was apparently unique in the respect that the products arising from the alkylamine portion of the molecule did vary with the nature of the group attached to the carbonyl carbon atom. This result is not, however, unexpected since the proposed dual path for the initial phase of the reaction would require formation of both the diazoether and the diacetate salt. Since this particular diacetate has already been shown to not protonate by ethanol to give the diazohydroxide (the normally presumed precursor to the diazo), the path involving carbonyl attack by base to form the diacetate would not be expected to yield the diazocompound. Therefore, only the path involving attack by the base on the nitroso nitrogen atom would produce the diazocyclopropane. For example, entries 1 and 3 in Table 2 show that as the amount of diethyl carbonate increases from 7 per

cent to 72 per cent, the amount of gas evolved (from the known spontaneous decomposition of the diazocyclopropane) decreases from 97 per cent to 31 per cent.

Another generality that becomes apparent upon examination of the Tables of Results is the fact that with the nitrosourethans and the nitrosoamides, the nature of the solvent used has a noticeable effect on the proportion of reaction that proceeds by initial attack of the base on the carbonyl carbon atom. For example, entries 9 and 10 in Table 2 show that attack by ethoxide on the carbonyl carbon atom of the nitrosobenzylurethan drops from 47 per cent with lithium ethoxide in ethanol to only 10 per cent with the same base in ether. This effect could be due to the change in polarity or protonicity, so the same reaction was conducted in other aprotic solvents of varying polarity in an attempt to determine the cause of this change. In ethyleneglycol dimethylether, acetone and dimethyl sulfoxide, again only small amounts of diethyl carbonate were detected (entries 12, 13 and 14 of Table 2). Thus, it appears that aprotic solvents favor attack of the base at the nitroso nitrogen atom while protic solvents seem to promote base attack at the carbonyl carbon atom. Entries 7 and 8 in Table 3 emphasize this point even more dramatically. These results suggest that there might exist some degree of coordination between the nitroso oxygen atom and the carbonyl

carbon in aprotic solvents, which can be destroyed by a hydrogen bonding solvent such as ethanol. Any coordination between these groups would tend to hinder attack by the base at the carbonyl position.

This effect could also create a partial positive charge on the nitroso nitrogen atom, perhaps enough to help promote attack of the negatively charged ethoxide anion at that position. There is, however, no strong evidence to support this suggestion.

Finally, it should be noted that steric effects due to both the size of the alkyl substituent and the base cation employed are involved in the determination of the mode of attack by base on nitrosourethanes. It can be seen from entries 11, 3, and 6 of Table 2 that with potassium carbonate in ethanol, the amount of diethyl carbonate formed increased significantly as the alkyl group varied from benzyl to cyclohexyl. Also, with the cyclohexyl derivative, the proportion of base attack at the carbonyl carbon atom increased with the size of the base cation employed (cf. entries 5, 7, and 8 in Table 2).

CHAPTER IV

EXPERIMENTAL

The melting points were taken in a Thomas Hoover hot-melt apparatus and are uncorrected. The infrared spectra were recorded with a Perkin-Elmer Infracord spectrophotometer and the ultraviolet spectra were recorded with a Cary 14. The elemental analyses were carried out by Galbraith Laboratories, Inc., Knoxville, Tennessee. Vapor phase chromatographic analyses were performed with an Aerograph Hy-Fi model 600-B.

Materials.--The solvents (anhydrous ethyl ether, petroleum ether, chloroform, acetone and tetrahydrofuran) used in this work were all Fisher Certified Reagents and were used without further purification, as were the benzaldehyde and the isoamyl alcohol. The ethyl carbamate (Matheson), the allyl acetate and the cyclohexylurea (K and K), the menthol and the naphthalene (Fisher Practical Grade), the benzylamine (Eastman Practical Grade) and the cyclopropanecarboxylic acid and the cyclobutanecarboxylic acid (Aldrich) were also used without further purification, as were the following Eastman White Label chemicals: diethyl

fumarate, ethyl chloroformate, cyclohexylamine, deoxybenzoin and diethyl carbonate. The dimethyl sulfoxide (Methesom) and the ethylene glycol dimethyl ether (Ansul) were freshly distilled before use.

Conditions used for V.P.C. analyses.--The two columns used for v.p.c. analyses were:

Column 1 - 7 per cent Carbowax 20M on 60/80 mesh Gas Chrom Z (5 ft. x 1/8 in.).

Column 2 - 20 per cent SE-30 on 60/80 mesh Gas Chrom Z (5 ft. x 1/8 in.).

The peak areas were determined with a disc-chart integrator, and specific conditions required to effect clean separations are listed below:

Compound Analyzed	Internal Standard	Gas Flow (lbs. N)	Temp	Column
Ethyl Carbamate	Menthol	15	110°	1
Diethyl Carbonate	Allyl Acetate	15	30°	1
Diethyl Carbonate	Isoamyl Alcohol	18	30°	2
Ethyl Benzoate	Naphthalene	20	115°	1
Ethyl Acetate	Diethyl Carbonate	9-24	30°	1
Benzyl Ethyl Ether	Naphthalene	20	115°	1

Preparation of N-nitroso-N-alkylureas.--The following general procedure for nitrosation of alkylureas has been found to give consistently good yields of product. In a typical preparation, 1.00 g (0.010 mole) of cyclopropylurea

was stirred in 15 ml. of anhydrous ether at -50° along with 0.82 g. (0.010 mole) of anhydrous sodium acetate. A solution of dinitrogen tetroxide (0.92 g., 0.010 mole) in ether (prepared by blowing the gas into a tared volumetric flask about one-half full with ether at -50° and noting the increase in weight) was then added with a syringe through a rubber septum. The blue color of the oxide slowly faded during 30 minutes of stirring, leaving a green solution which changed to yellow as the temperature was allowed to raise to -20°. After filtering off the inorganic residue, the filtrate was then washed with 5 per cent aqueous sodium bicarbonate to remove the acetic acid, then with water, and finally dried over anhydrous magnesium sulfate. Filtration with suction followed by removal of the ether from the filtrate on a rotary evaporator gave the product as a yellow solid, m.p. 95-98° (dec.). By not removing quite all of the ether, the nitrosourea could be precipitated by the addition of pentane. This procedure gave yellow crystals, m.p. 104° (dec.), in a yield of 0.95 g. (74%). Recrystallization from a chloroform-pentane solvent mixture gave fine yellow needle crystals, m.p. 108° (dec.).

Anal. Calcd. for $C_4H_7N_3O_2$: C, 37.21; H, 5.43; N, 32.56. Found: C, 36.87; H, 5.67; N, 32.87.

This compound has been reported earlier to have a melting point of 86° (dec.).

The following table gives pertinent data concerning the preparations effected.

R-N-C-NH_2 (O)	Melting Point	Reported Melting Point	Yield
R =	108	86[21]	74
R =	66-67	67-69[14]	39
R =	114-115	114-115[4]	78
R =	116	116[22]	24
R = ϕCH_2^-	100-101	101[2]	66

Preparation of N-nitroso-N-alkylamides.--The general procedure of White[20] was employed in the preparation of the nitrosoamides from the corresponding alkylamides. In a typical preparation, N-benzylbenzamide (2.11 g., 0.010 mole) was stirred in glacial acetic acid at 0-5° along with 1.64 g. (0.020 mole) of anhydrous sodium acetate, and 0.92 g. (0.010 mole) of dinitrogen tetroxide in ether was added in portions. In most cases, the nitrosoamides were obtained as yellow oils which were checked for purity with thin layer chromatography and by examination of the infrared spectra for loss of the N-H absorption maxima at 2.8-2.9 microns.

$R_1-\overset{O}{\overset{\|}{N}}-\overset{O}{\overset{\|}{C}}-R_2$	Observed Melting Point	Reported Melting Point	Yield	Reference
$R_1 = \phi CH_2-$, $R_2 = \phi$	45-47°	46-47°	91	23
$R_1 = \phi CH_2-$, $R_2 = CH_3-$	(oil)	-	93	24
$R_1 =$ $R_2 = \phi$	(oil)	-	84	-

Preparation of N-nitroso-N-alkylurethans.--The nitrosourethans shown below were prepared in nearly quantitative yields by the addition of an ether solution of dinitrogen tetroxide to an ether solution of each of the urethans stirring at -30°.

In a typical preparation, 3.58 g. (0.0020 mole) of benzylurethan was dissolved in 20 ml. of anhydrous ether which was stirring at -30° over 1.64 g. (0.0020 mole) of anhydrous sodium acetate. To this solution was added a solution of 1.84 g. (0.0020 mole) of dinitrogen tetroxide in ether (prepared by blowing the gaseous oxide into a tared volumetric flask containing a little ether at -50° and recording the increase in weight). Stirring was continued at -30° for 30 minutes or until the solution turned from blue to yellow. Warming to 0° over 10 minutes completed any slow reactions. After filtering off the inorganic salts, this solution was then washed with 5 per cent aqueous sodium bicarbonate, then with water, and finally dried over sodium sulfate. Removal of the solvent on a rotary

evaporator gave 3.90 g. (94%) of a yellow oil which showed no N-H infrared absorption at 2.85 microns, n_D^{23} = 1.5155 (lit.[25] n_D^{25} = 1.5166).

R-N(-C=O)-COC$_2$H$_5$	n_D^{23}	Reported n_D (temp.)	Yield
R =	-	-	88
R =	-	-	91
R =	1.4716	1.4702 (20°)[15]	93
R = $C_6H_5CH_2$-	1.5155	1.5166 (25°)[25]	94

Benzylurethan.--Benzylurethan was prepared by the method of Kurtz and Nisenann,[25] using 53.5 g. (0.50 mole) of benzyl amine, 20 g. (0.5 mole) of sodium hydroxide, and 54.3 g. (0.50 mole) of ethyl chloroformate. The crude product obtained was distilled in vacuo to give 65 g. (76%) of a clear liquid, b.p. 103° (2 mm. Hg.), which soon crystallized to give a white solid, m.p. 43-44° (lit.[25] m.p. 44°).

Cyclobutanecarbonyl chloride.--Cyclobutanecarbonyl chloride was prepared by mixing 10.0 g. (0.10 mole) of cyclobutanecarboxylic acid with 20.0 g. (0.17 mole) of thionyl chloride according to the method of Applequist and

McGreer.[14] The distilled product came over between 130-140° C. (Lit.[14] 130-140) in a yield of 10.5 g. (77%).

Cyclobutylurea.--Cyclobutylurea was prepared according to the general scheme reported previously[4] from cyclobutanecarbonyl chloride. The intermediate cyclobutanecarbonyl azide and isocyanate were not isolated. The cyclobutylurea was isolated as fine white needle crystals, m.p. 166-171°, in a yield of 6.3 g. (55% based on starting acid). This crude sample was recrystallized from ethyl acetate to give large white needle crystals, m.p. 170-171° (Lit.[14] m.p. 170.5-171°).

Cyclopropylurea.--Cyclopropylurea was prepared by the general method previously reported,[4] with one exception. The intermediate cyclopropanecarboxylic acid chloride was fractionally distilled from unreacted thionyl chloride. The acid chloride was collected at 47° (55 mm.) (the thionyl chloride distilled at 33-35° under 65-75 mm.). The desired urea was obtained as needle crystals melting at 124° (24%) (Lit.[21] m.p. 123-124°).

Cyclohexylurethan.--Cyclohexylurethan was prepared by the method of Kurtz and Wiemann.[25] Cyclohexyl amine (49.6., 0.50 mole) was diluted with 150 ml. of anhydrous ethyl ether and stirred over a solution of 20 g. (0.50 mole) of sodium hydroxide in 100 ml. of water with a paddle stirrer. After

[illegible] to 5°, 54.3 g. (0.50 mole) of benzyl [illegible] in 50 ml. of anhydrous ethyl ether was added dropwise over three hours, with care taken to keep the temperature near 5°. Removal of the solvent on a rotary evaporator gave 82 g. (96%) of white solid, m.p. 48-53°. Recrystallization from methanol-water without heating gave white needles, m.p. 53-54° (Lit.[15] m.p. 56-56.5°, solidified from distilled liquid).

N-Benzylacetamide.—N-Benzylacetamide was prepared by reacting 10.7 g. (0.100 mole) of benzyl amine with an excess of acetic anhydride (25 ml.) containing 2 drops of concentrated sulfuric acid. External cooling was required to keep the reaction near room temperature. After stirring for one-half hour, this solution was poured into 35 ml. of water containing a few drops of concentrated hydrochloric acid and stirred for three hours. The resulting solution was extracted with benzene and the extracts were washed with 5 per cent aqueous sodium bicarbonate, then water, and finally dried over anhydrous magnesium sulfate. After filtering the dry benzene solution, the solvent was removed on a rotary evaporator to give a clear liquid which crystallized upon standing a few minutes to give 12.8 g. (85%) of white crystals, m.p. 60-61° (Lit.[6] m.p. 61°).

N-Benzylbenzamide.--N-Benzylbenzamide was prepared by reacting 10.7 g. (0.100 mole) of benzyl amine with 14.10 g. (0.100 mole) of benzoyl chloride in a solution of 30 ml. of anhydrous pyridine and 100 ml. of dry benzene. After warming the solution at 60-80° on a steam bath for three hours, it was poured into 200 ml. of water and this mixture was stirred for two hours. The benzene layer was separated, washed with 1 N. hydrochloric acid, 5 per cent aqueous sodium bicarbonate, water and finally dried over anhydrous magnesium sulfate. This dry benzene solution was filtered and concentrated to about 50 ml. on a rotary evaporator, at which time a white solid began to precipitate. After allowing crystallization to take place for two hours, the resulting product was obtained by suction filtration as white crystals, m.p. 104-105° (Lit.[6] m.p. 105°), in a yield of 17.1 g. (81%).

Benzylurea.--Benzylurea was prepared by the method of Boivin and Boivin,[26] using 5.15 g. (0.050 mole) of N-nitroso-N-methylurea and 5.35 g. (0.050 mole) of benzyl amine. The product was obtained as white needle crystals, m.p. 146-147° (Lit.[26] m.p. 147-147.5°), which separated from the aqueous reaction mixture upon cooling, in a yield of 5.05 g. (68%).

Benzyl ethyl ether.--Benzyl ethyl ether was prepared by adding 5.13 g. (0.030 mole) of benzyl bromide to a freshly prepared solution of 0.70 g. (0.030 mole) of sodium

[illegible] precipi-
[illegible] for ea, but the solution was refluxed for [illegible] before
filtering off the sodium bromide. After evaporation of the
solvent on a rotary evaporator, the residual yellow oil was
distilled in vacuo to give 2.80 g. (69%) of clear liquid,
b.p. 77-78°/18 mm. Hg. and n_D^{22} = 1.4948 (Lit.[5] b.p. 78°/18
mm. Hg., n_D^{20} = 1.4955).

2,2-Diphenylcyclopropylurethan.--2,2-Diphenylcyclo-
propylurethan was prepared by reacting absolute ethanol
with 2,2-diphenylcyclopropyl isocyanate (prepared from 2,2-
diphenylcyclopropane carboxylic acid by a method reported
earlier[4]). 2,2-Diphenylcyclopropane carboxylic acid (16.5
g., 0.070 mole) was converted to the corresponding iso-
cyanate, and 12.9 g. (0.28 mole) of absolute ethanol was
added to the resulting benzene solution and refluxed for
six hours. After removing the benzene with a rotary evapo-
rator, the viscous liquid obtained was pumped under a vacuum
(1 mm. Hg.) overnight to effect crystallization. This crude
product was obtained as light brown crystals, m.p. 65-68°
in a yield of 13.5 g. (68%). Recrystallization from aqueous
methanol gave white needle crystals, m.p. 74-75°.

Anal. Calcd. for $C_{18}H_{19}NO_2$ C, 76.87; H, 6.76; N,
4.98. Found: C, 77.02; H, 6.68, N, 5.13.

Stability of ethyl benzoate to lithium hydroxide in ethyl alcohol.—Ethyl benzoate (0.300 g., 0.0020 mole) was stirred in 10 ml. of absolute ethyl alcohol containing 0.048 g. (0.0020 mole) of dissolved lithium hydroxide for eight hours at room temperature. When the solvent was removed on a rotary evaporator and the residue was triturated with ether, 0.045 g. of white powder was obtained by suction filtration. An infrared spectrum of this solid was superimposable with that of a known sample of lithium hydroxide. The filtrate was then evaporated to give 0.253 g. of a clear liquid, the infrared spectrum of which was identical to that of pure ethyl benzoate (84% recovery).

Attempted trimerization of methyl isocyanate.—Methyl isocyanate was prepared by the reaction of diazomethane and isocyanic acid. A benzene solution of diazomethane was prepared by the base induced decomposition of N-nitroso-N-methylurea.[11] Through this solution was bubbled a stream of isocyanic acid (generated by the thermal depolymerization of cyanuric acid at 380–400°) in dry argon until the yellow color just disappeared. The resulting benzene solution of methyl isocyanate was then heated to reflux. The strong odor of isocyanate was still present after two hours, so refluxing was continued overnight. When the benzene was then removed with a rotary evaporator, a negligible amount of residue remained in the reaction flask.

Determination of cyanuric acid from the thermal decomposition of N-nitroso-N-(2,2-diphenylcyclopropyl)urea in n-heptane.--N-Nitroso-N-(2,2-diphenylcyclopropyl)urea (0.281 g., 0.0010 mole) was stirred in 15 ml. of n-heptane and heated to 90°. When gas evolution had ceased and the yellow color of the nitrosourea had disappeared, the solution was cooled and filtered with suction. The white solid obtained was added to that which was scooped from the neck of the flask to give 0.035 g. (0.00027 mole, 81.6%) of product stable to 280°. Infrared spectra of this material (KBr and Nujol mull) were identical to the corresponding spectra of a known sample of cyanuric acid (the spectra vary depending on the sampling agent used).

Reaction of diazomethane with isocyanic acid.--Through an ether solution of diazomethane (0.0175 mole in 60 ml., prepared from N-nitroso-N-methyl p-toluenesulfonamide[27]) was bubbled a slow stream of isocyanic acid (generated by the thermal depolymerization of cyanuric acid at 380-400°) in dry argon. The yellow color disappeared in two or three minutes, and the resulting colorless solution had a very strong odor, presumably of methyl isocyanate. Since the reaction of methyl isocyanate with aniline has been reported to give a solid derivative,[28] this solution was then poured into a benzene solution of about a three-fold molar excess of aniline (4.88 g., 0.0525 mole). After standing overnight,

removal of the solvent with a rotary evaporator left a small amount of unreacted aniline and a white solid. This mixture was taken up in ether, washed with 1 N aqueous hydrochloric acid, 5 per cent aqueous sodium bicarbonate, water, and dried over anhydrous magnesium sulfate. Evaporation of this dry ether solution gave a white solid, m.p. 142-150°. Recrystallization from a hot ethanol-water solvent mixture gave white plates, m.p. 151° (Lit.[28] m.p. 151°) in a yield of 0.700 g. (0.00470 mole), which corresponds to 27 per cent if quantitative formation of the isocyanate is assumed.

Reaction of sodium carbamate with p-toluenesulfonic acid in refluxing benzene.—Sodium carbamate (0.083 g., 0.0010 mole) was ground in a small amount of THF for a few minutes and this paste diluted with 15 ml. of benzene. The resulting solution was heated to reflux and 0.190 g. (0.0010 mole) of p-toluenesulfonic acid (monohydrate) dissolved in 2 ml. of THF was added with stirring. After one hour, the solution was filtered to give 0.235 g. of white solid. An infrared spectrum of this product showed it to be a mixture of sodium p-toluenesulfonate and ammonium p-toluenesulfonate (compared with a spectrum of an authentic mixture of these materials). None of the absorptions characteristic of cyanuric acid were observable.

Reaction of lithium carbamate with p-toluenesulfonic acid in refluxing benzene.--Lithium carbamate (0.067 g., 0.0010 mole) was treated with 0.190 g. (0.0010 mole) of p-toluenesulfonic acid under the same conditions shown before for the protonation of sodium carbamate. Similar to the case of sodium carbamate, only ammonium p-toluenesulfonate and lithium p-toluenesulfonate were observed as products.

Attempted thermal decomposition of N-nitroso-N-(2,2-diphenylcyclopropyl)-N',N'-dimethylurea in n-heptane.--N-Nitroso-N-(2,2-diphenylcyclopropyl)-N',N'-dimethylurea[8] (0.309 g., 0.0010 mole) was stirred in 15 ml. of n-heptane which was subsequently heated to reflux. During three hours, the solution turned from yellow to deep orange in color, but there was no net gas evolution observed. After removing the solvent with a rotary evaporator, an infrared spectrum was taken on the gummy material remaining. There was no peak at 5.2 u typical of diphenylallenes. However, there did appear to be considerable loss of starting material, with an unknown olefin as one of the products.

Preparation of lithium carbamate.--To about 15 ml. of liquid ammonia and two small crystals of anhydrous ferric nitrate stirring in a 50 ml. round bottom flask was added 0.70 g. (0.10 mole) of lithium wire in small pieces. Stirring was continued for one hour yielding a dark grey suspension through which anhydrous carbon dioxide was bubbled.

As the volume of the solution decreased, anhydrous ether was slowly added over 30 minutes to hold a constant volume. The resulting light brown suspension was filtered and the solid pumped under vacuum to remove any remaining ammonia. This light tan powder (3.90 g., 0.0795 mole - 79.5%) was stable to 280°. This procedure was developed from the method of Elsir[29] in which he prepared the ammonium carbamate separately from gaseous carbon dioxide and ammonia before reaction with the metal amide. Significant infrared absorptions are (KBr): 2.86, 2.95, 3.10, 6.20, 6.30, 6.41, 7.05, 8.48, 8.90, and 12.10 (microns). A satisfactory analysis could not be obtained due to varying amounts of solvated ammonia.

Sodium carbamate.--Sodium carbamate was prepared by the method of Bernard,[30] in which ammonium carbamate was prepared by reacting liquid ammonia with solid carbon dioxide, and allowed to react over a period of hours with sodium chloride initially dissolved in liquid ammonia. A small amount of sodium chloride contaminated the white solid obtained. Characteristic infrared absorption maxima are (KBr): 2.90, 3.10, 6.00, 6.20, 6.30, 7.15, 8.85, and 12.18 (microns).

Anal. Calcd. for CH_2NO_2Na: C, 12.90; H, 2.15; N, 15.05. Found: C, 12.14, H, 2.33; N, 15.42. (Adjusted from values actually found to compensate for the sodium chloride present. found 6.52 % Cl, corresponding to 10.75 % NaCl).

Reaction of diazomethane with cyanuric acid.--Cyanuric acid (0.500 g., 0.00387 mole) was stirred in anhydrous ether at 0° and an ether solution of diazomethane added (0.163 g., 0.00387 mole). The yellow color of diazomethane was gone after 30 minutes of stirring, so more diazomethane was added until the color persisted. The resulting solution was filtered and the solvent removed from the filtrate with a rotary evaporator. A white solid remained, m.p. 171-173°, which was recrystallized from hot ethanol-water to give 0.400 g. (0.0023⅓ mole, 61%) of white crystals, m.p. 173-174° (reported,[5] m.p. 174-175°).

Lithium ethoxide.--Lithium ethoxide was prepared by the method of Brown and coworkers[31] with the exception that a two-fold molar amount of ethanol was used instead of the reported molar amount in order to increase the yield. The product was then heated on a steam bath under vacuum (2 mm) to remove the last traces of ethanol. This procedure gave a white powder whose infrared spectrum showed none of the peaks characteristic of lithium carbonate, lithium hydroxide or ethanol. Addition of sodium hydride to an ether suspension of this product gave no gas evolution, which indicates that there is no ethanol remaining as the alcoholate. A sample of this powder was weighed accurately, dissolved in distilled water, and titrated by first adding an excess of standard dilute hydrochloric acid and then back titrating

with standard dilute sodium hydroxide. In two successive runs, values of 50.4 and 51.6 were obtained for the equivalent weight of lithium ethoxide (calc. 51.9). The infrared spectrum was identical to that obtained by Brown and coworkers.[31]

Decomposition of N-nitroso-N-(2,2-diphenylcyclopropyl)urea with lithium ethoxide in ethyl ether.--N-nitroso-N-(2,2-diphenyloylcopropyl)urea (0.281 g., 0.0010 mole) was stirred in 15 ml. of anhydrous ethyl ether at 0° and 0.052 g. (0.0010 mole) of lithium ethoxide quickly added. After stirring at 0° for 20 minutes, 18 ml. (75%) of gas had been collected and gas evolution had ceased. The reaction mixture was filtered to give 0.055 g. of white solid. After removing the solvent from the filtrate with a rotary evaporator, the residual oil was triturated with pentane, which caused some solid to precipitate. Filtration of the pentane extracts gave 0.025 g. of white solid material, whose infrared spectrum was identical to that of a sample of lithium 2,2-diphenylcyclopropyldiazotate. When the pentane was removed from the filtrate, 0.145 g. (76%) of oil remained whose infrared spectrum was superimposable with that of diphenyl allene. A closer examination of the 0.055 g. of white solid initially obtained revealed the following: trituration with chloroform for 30 minutes and filtration with suction gave 0.033 g. (73%) of a white solid whose infrared spectrum was

identical to that of a sample of lithium cyanate, and removal of the chloroform with a rotary evaporator gave 0.017 g. more of the lithium 2,2-diphenylcyclopropyldiazotate (total yield, 0.042 g., 17%).

Stability of lithium 2,2-diphenylcyclopropyldiazotate to lithium ethoxide in ethanol.--Lithium 2,2-diphenylcyclopropyldiazotate (0.244 g., 0.0010 mole) was stirred for one hour at 0° in 10 ml. of absolute ethanol containing 0.052 g. (0.0010 mole) of lithium ethoxide. The ethanol was removed by evaporation under high vacuum. The white solid obtained as residue (0.285 g. 96% recovery) exhibited infrared absorptions that were consistent with a mixture of the diazotate and lithium ethoxide.

Stability of lithium 2,2-diphenylcyclopropyldiazotate to isocyanic acid in tetrahydrofuran at zero degrees.--Lithium 2,2-diphenylcyclopropyldiazotate (0.180 g., 0.00059 mole) was stirred in 15 ml. of anhydrous tetrahydrofuran at 0° for a few minutes before adding a solution of isocyanic acid (0.023 g., 0.00059 mole) in 5 ml. of tetrahydrofuran. After stirring for 30 minutes at 0°, the solvent was removed on a rotary evaporator leaving a quantity of solid whose infrared spectrum was identical to that of the starting diazotate, with none of the absorptions characteristic of lithium cyanate.

Stability of lithium carbamate to reaction conditions.--Lithium carbamate was checked for stability to the following sets of conditions by stirring 0.069 g. (0.0010 mole) in anhydrous ethyl ether for 30 minutes, evaporating the solvent quickly under high vacuum, and then immediately taking the infrared spectrum of the residue:

-0.052 g. (0.0010 mole) of lithium ethoxide.

-0.024 g. (0.0010 mole) of lithium hydroxide.

-0.281 g. (0.0010 mole) of N-nitroso-N-(2,2-diphenylcyclopropyl)urea.

-0.018 g. (0.0010 mole) of water.

-0.049 g. (0.0010 mole) of lithium cyanate.

-the solvent only.

In each case, the lithium carbamate was recovered unchanged and there was no gas evolution with the nitrosoures.

Stability of sodium carbamate to reaction conditions.--Sodium carbamate was checked for stability to the same sets of conditions as was lithium carbamate, since a satisfactory analysis of lithium carbamate could not be obtained. In every case, the sodium carbamate was recovered in essentially quantitative yield.

Reaction of lithium carbamate with p-toluenesulfonic acid.--Lithium carbamate (0.052 g., 0.0010 mole) was stirred in 10 ml. of anhydrous tetrahydrofuran at room temperature for one hour and then cooled to -50°. p-Toluenesulfonic

acid (monohydrate) (0.190 g., 0.0010 mole) dissolved in 5 ml. of anhydrous tetrahydrofuran at -50° was quickly added and the resulting solution stirred at -50° for one hour. The reaction mixture was then warmed to room temperature and the solvent was removed on a rotary evaporator to give 0.235 g. of white solid. The infrared spectrum of this solid indicated that it was a mixture of ammonium tosylate, lithium tosylate, and some unreacted lithium carbamate (by comparison of the spectra of the known materials).

Reaction of sodium carbamate with p-toluenesulfenic acid.--Sodium carbamate was treated with p-toluenesulfenic acid in a manner identical to that shown before for lithium carbamate, and the same results were obtained.

Sodium cyanate.--Sodium cyanate was prepared by bubbling a stream of isocyanic acid in dry argon (generated by the thermal depolymerization of cyanuric acid at 380-400°) through a rapidly stirred suspension of sodium ethoxide in anhydrous ethyl ether at 0°. The product obtained by filtering the reaction mixture showed infrared absorptions identical to those reported by Rao.[32]

Lithium cyanate.--Lithium cyanate was prepared by bubbling a stream of isocyanic acid in argon (generated by the thermal depolymerization of cyanuric acid at 380-400°) through a rapidly stirred suspension of lithium ethoxide in anhydrous ethyl ether at 0°. The lithium cyanate obtained

showed some infrared absorption characteristic of lithium hydroxide. The product was purified by stirring in absolute ethanol and then added ether to precipitate out the lithium hydroxide. Filtration and evaporation of the solvent from the filtrate gave a white solid whose infrared spectrum was very similar to that of a sample of sodium cyanate. The infrared absorptions (KBr) appeared at 4.40, 7.60 and 8.20 microns.

Reaction of pyrrolidine with isocyanic acid.--To a stirred solution of pyrrolidine (0.280 g., 0.0040 mole) in 10 ml. of anhydrous ether at 0° was added a solution of isocyanic acid (0.172 g., 0.0040 mole) in tetrahydrofuran. An immediate precipitate formed and there was no more changes over 30 minutes. The solution was filtered with suction giving 0.530 g. (94.5%) of white solid, m.p. 220-221° (Lit.[33] m.p. 218°). The infrared spectrum of this material compared exactly with that of the N-pyrolidinylcarboxamide isolated from the reaction of pyrrolidine with N-nitroso-N-(2,2-diphenylcyclopropyl)urea reported herein.

Attempted decomposition of N-nitroso-N-(2,2-diphenylcyclopropyl)-N',N'-dimethylurea with lithium ethoxide.--N-nitroso-N-(2,2-diphenylcyclopropyl)-N',N'-dimethylurea (0.309 g., 0.0010 mole) was stirred in 25 ml. of anhydrous ethyl ether at 0° and 0.052 g. (0.0010 mole) of lithium ethoxide added quickly. After stirring at that temperature

for an hour and observing no gas evolution, the m[illegible] was stirred at room temperature overnight. By then cooling the system back to 0°, it was evident that there had been no net gas evolution. Filtration and removal of the solvent from the filtrate with a rotary evaporator left a yellow gummy solid. Addition of 1 ml. of ether followed by 5 ml. of pentane dropwise precipitated a yellow solid (0.290 g., 94%), m.p. 85-87° whose infrared spectrum was identical to that of a sample of the starting nitrosourea.

Reaction of N-nitroso-N-(2,2-diphenylcyclopropyl)urea with lithium hydroxide.--To a solution of 0.300 g. (0.00107 mole) of N-nitroso-N-(2,2-diphenylcyclopropyl)urea in 30 ml. of anhydrous ether stirred at 0° was added 39 mg. (1.5 equivalents) of lithium hydroxide. Nitrogen slowly evolved for five hours (21.2 ml., 78.5%) after which the reaction mixture was filtered. An infrared spectrum (KBr) of the white solid (129 mg.) was consistent with a mixture of lithium 2,2-diphenylcyclopropyldiazotate and lithium cyanate. The filtrate was evaporated to an oil (183 mg.) whose infrared spectrum (film) was identical to that of 1,1-diphenylallene.

Reaction of N-nitroso-N-(2,2-diphenylcyclopropyl)urea with varying amounts of lithium ethoxide.--In order to demonstrate that a full molar quantity of lithium ethoxide

was needed to decompose the nitrosoureas, the amou[illegible] were varied in a series of decomposition reactions. To 0.281 g. (0.0010 mole) of N-nitroso-N-(2,2-diphenylcyclopropyl)urea stirring in 15 ml. of anhydrous ether at 0° was added lithium ethoxide in the following partial molar quantities. In each case, stirring was continued until gas evolution had ceased and the solution then filtered. When the solvent was removed on a rotary evaporator, the gummy yellow material was triturated with pentane to give the unreacted solid nitrosourea and a solution of any diphenylallene formed. After evaporation of the pentane, the amount of diphenylallene was determined by weighing.

Amount LiOEt (%)	Gas Evolution (%)	Diphenylallene Isolated (%)	Recovered Nitrosourea (%)	Dimerate Isolated (%)
25	22	18	78	0
50	47	42	53	0
75	61	52	36	3
100	76	75	0	17

Salts of p-toluenesulfonic acid.--The sodium, lithium and ammonium salts of p-toluenesulfonic acid were prepared by neutralizing an ethyl alcohol solution of the acid respectively with solutions of sodium hydroxide, lithium

ethoxide and ammonia in ethyl alcohol. The solid salts were isolated by removal of the solvent with a rotary evaporator.

The base induced decomposition of N-nitroso-N-benzylurea.--In each run shown in Table 1, 0.358 g. (0.0020 mole) of N-nitroso-N-benzylurea was dissolved in 15 ml. of the solvent stirring at 0° and the base, either lithium ethoxide (0.104 g., 0.0020 mole) or potassium carbonate (0.276 g., 0.0020 mole) was quickly added. Stirring was continued until gas evolution ceased and the reaction solution was filtered. The filtrate was then analysed on the v.p.c. for ethyl carbamate, using menthol as the internal standard. Conditions of the v.p.c. analysis allow an accuracy of ± 2 per cent.

The base induced decomposition of N-nitroso-N-(2,2-diphenylcyclopropyl)urethan.--In each decomposition listed in Table 2, 0.620 g. (0.0020 mole) of N-nitroso-N-(2,2-diphenylcyclopropyl)urethan was dissolved in 15 ml. of the solvent stirring at room temperature. The base, either lithium ethoxide (0.104 g., 0.0020 mole) or potassium carbonate (0.276 g., 0.0020 mole) was then quickly added and the system monitored for gas evolution. When the evolution of gas ceased, the reaction mixture was filtered if necessary and the filtrate was analysed for diethyl carbonate on the v.p.c., using isoamyl alcohol as the internal standard. An accuracy of ± 2 per cent is allowed by these conditions.

The base induced decomposition of N-nitroso-N-cyclohexylurethan.--With each example shown in Table 2, 0.400 g. (0.0020 mole) of N-nitroso-N-cyclohexylurethan was stirred in 15 ml. of the solvent and 0.0020 mole of the base (0.104 g. of lithium ethoxide, 0.276 g. of potassium carbonate, 0.078 g. of potassium in 5 ml. of ethanol, or 0.046 g. of sodium in 5 ml. of ethanol) was added. When the gas evolution ceased, the reaction solutions were filtered if necessary and then analyzed on the v.p.c. (Column 2) for diethyl carbonate, using isoamyl alcohol as the internal standard. V.p.c. conditions here allow an accuracy of ± 2 per cent.

The base induced decomposition of N-nitroso-N-benzylurethan.--In each case, 0.358 g. (0.0020 mole) of N-nitroso-N-benzylurethan was stirred in 15 ml. of the solvent at room temperature, and the base (0.104 g., 0.0020 mole of lithium ethoxide or 0.276 g., 0.0020 mole of potassium carbonate) was added quickly. Gas evolution was followed until it ceased, the phenyldiazomethane was decomposed with glacial acetic acid while checking for gas evolution, and the resulting solution was analyzed for diethyl carbonate on the v.p.c., using allyl acetate as an internal standard. Conditions of analysis here allow an accuracy of ± 3 per cent.

Decomposition of N-nitroso-N-cyclobutylurea with lithium ethoxide in ether.--To 15 ml. of anhydrous ether stirring at 0° was added 0.286 g. (0.0020 mole) of N-nitroso-N-cyclobutylurea. Lithium ethoxide (0.104 g., 0.0020 mole) was dissolved in 2 ml. of absolute ethanol and this solution was quickly added to the ether solution above. Gas evolution was rapid, with 35 ml. (78%) being evolved in 5 minutes. After filtering the reaction mixture with suction to give 0.032 g. (65%) of lithium cyanate, the filtrate was analyzed for ethyl carbamate with the v.p.c., using 0.0026 g. of menthol as the internal standard. No ethyl carbamate was observed, while 0.0009 g. (0.5%) would easily have been detected.

The base induced decomposition of N-nitroso-N-cyclohexylurea.--In each example shown in Table 1, 0.171 g. (0.0010 mole) of N-nitroso-N-cyclohexylurea was dissolved in 15 ml. of the solvent stirring at 0° and the base, either lithium ethoxide (0.052 g., 0.0010 mole) or potassium carbonate (0.138 g., 0.0010 mole) was quickly added. Stirring was continued until gas evolution ceased and the reaction solution was filtered. The filtrate was then analyzed on the v.p.c. for ethyl carbamate, using menthol as the internal standard. V.p.c. conditions here allow an accuracy of ± 2 per cent.

The base induced decomposition of N-nitroso-N-benzyl-benzamide.--In each run listed in Table 3, 0.480 g. (0.0020 mole) of N-nitroso-N-benzylbenzamide was stirred in 15 ml. of the solvent at room temperature. The base, either lithium ethoxide (0.104 g., 0.0020 mole) or potassium carbonate (0.276 g., 0.0020 mole), was then quickly added and the closed system monitored for gas evolution. After gas evolution had ceased, the reaction mixture was filtered if necessary and benzaldehyde was added to decompose the phenyldiazomethane. The resulting solution was then analyzed for ethyl benzoate with the v.p.c., using naphthalene as the internal standard. Since benzyl ethyl ether was a product of the runs made in ethyl alcohol, its yield was also determined on the v.p.c. using the naphthalene as the internal standard. For the runs made in alcohol, the solvent had to be evaporated on a rotary evaporator in order to check the salts present. The alkali benzoates were analyzed by dissolving them in water, acidifying with 1 N hydrochloric acid, and extracting the benzoic acid with ether. V.p.c. conditions allow an accuracy of ± 3 per cent on both analyses.

Preparation of phenyldiazomethane from the base decomposition of N-nitroso-N-benzylamine derivatives.--Phenyldiazomethane was prepared from three derivatives of N-nitroso-N-benzylamine by decomposition with lithium ethoxide or potassium carbonate in ethanol, ether, or hexane. In each

rum, the gas evolved during formation of the diazo was monitored and is recorded in Table 4 as that evolved during the first step. The yield of diazo compound was determined by decomposing the red solutions with glacial acetic acid and following the nitrogen evolution. In every case, the sum of the volumes of gas evolved corresponded to quantitative evolution of nitrogen. The specific conditions employed are recorded in Table 4 along with the yields of phenyldiazomethane produced.

Reaction of phenyldiazomethane with benzaldehyde.--A solution of phenyldiazomethane was prepared by decomposing 1.79 g. (0.010 mole) of N-nitroso-N-benzylurea dissolved in 50 ml. of absolute ethanol at -20° with 0.52 g. (0.010 mole) of lithium ethoxide. Gas evolution ceased in 5-10 minutes after 81 ml. (34%) had been collected. The solution was then warmed to room temperature and 1.06 g. (0.010 mole) of benzaldehyde (freshly distilled) was added with stirring. Stirring was continued for one hour, during which time 156 ml. of gas were evolved (65%). After removing the ethanol with a rotary evaporator, the residual oil was taken up in ether and washed twice with 10 ml. of 40 per cent aqueous sodium bisulfite solution, once with water, and dried over anhydrous magnesium sulfate. Removal of the ether on a rotary evaporator gave a crude white solid, m.p. 53-55° in a yield of 0.94 g. (74%, based on the assumption that 0.0065

mole of diazo was present). Recrystallization from methanol gave white plates, m.p. 55-56° (Lit.[34] m.p. 55-56°). The infrared spectrum of this material was identical to that of a known sample of desoxybenzoin.

A similar procedure was used to prepare phenyldiazomethane from N-nitroso-N-benzylurethan and N-nitroso-N-benzylbenzamide, and the same results were obtained with small variation of yields.

1-Benzoyl-3,4-dicarbethoxy-5-cyclopropyl-2-pyrazoline.--N-nitroso-N-cyclopropylurea (0.516 g., 0.00400 mole) was dissolved in 15 ml. of diethyl fumarate and stirred at 50-60° overnight while collecting evolved gases in a graduated tube. A colorless solution resulted with negligible gas evolution. This solution was passed through a column of Woelm acid washed alumina (15 mm. x 18 cm.) using pentane as the eluent. When all of the unreacted diethyl fumarate had been removed, the eluent was changed to ether containing 2 per cent methanol. About 100 ml. of solvent removed the pyrazoline from the column. The solvent was then removed on a rotary evaporator to give an oil which readily turned yellow on exposure to air. This oil was dissolved in 5 ml. of anhydrous pyridine and 1 ml. of benzoyl chloride added before refluxing overnight. The resulting dark solution was poured into water and stirred for three hours to remove the unreacted acid chloride. Extraction

with ether, followed by washing the extracts with 5 per cent aqueous hydrochloric acid, 5 per cent aqueous sodium bicarbonate, and then with water gave a deep red oil when the dried solvent was evaporated. This oil was chromatographed over Woelm acid washed alumina using ether as the eluent. Eight samples were collected, with thin layer chromatography showing the second to be essentially pure. Scratching of this oil under 95 per cent ethanol at dry ice temperature gave a white precipitate. Suction filtration gave a white solid, m.p. 90-92°, which was recrystallized from ethanol to give 0.0500 g. of white needles, m.p. 92-93°. This material exhibited ultraviolet absorption maxima in methanol at 237 mμ (ε = 6,830) and 302 mμ (ε = 14,200). Significant infrared absorptions are (KBr) 5.73, 5.90, 6.03, and 6.34 (microns).

Anal. Calcd. for $C_{18}H_{20}N_2O_5$: C, 62.78; H, 5.85; N, 8.13. Found: C, 62.57; H, 5.69; N, 8.14.

1-Benzoyl-3,4-dicarbethoxy-5-cyclohexyl-2-pyrazoline.--N-nitroso-N-cyclohexylurethane (4.00 g., 0.020 mole) was diluted with 10 ml. of diethyl fumarate and, while stirring at room temperature, 1.04 g. (0.020 mole) of lithium ethoxide was added in a few portions. This solution was then stirred overnight at room temperature. After diluting the resulting solution with ethyl ether, it was washed twice with 5 per cent aqueous sodium bicarbonate,

once with water, and dried over anhydrous magnesium sulfate. When the ether had been removed on a rotary evaporator the fumarate solution was chromatographed over alumina (Woelm, acid washed, column 20 mm. x 40 cm.) using hexane as eluent for the fumarate which came through rapidly. Elution with ether containing 1 per cent methanol gave 150 ml. of solution which was reduced to a yellow oil with a rotary evaporator. An infrared spectrum of this oil showed significant absorptions at 2.95, 5.8 (broad) and 6.45 (microns), indicating that the 2-pyrrolone had been formed. Attempts to crystallize this oil were unsuccessful, so the benzoyl derivative was prepared by reacting the oil in refluxing anhydrous pyridine with 2 ml. of benzoyl chloride. After refluxing overnight, the resulting solution was stirred in 50 per cent ethanol-water to hydrolyze the benzoyl chloride. After refluxing overnight, the resulting solution was stirred in 50 per cent ethanol-water to hydrolyze the benzoyl chloride, and the ethanol was removed with a rotary evaporator. This aqueous mixture was extracted with ether, and the extracts washed twice with 1 N hydrochloric acid, twice with 5 per cent aqueous sodium bicarbonate, and once with water before drying over anhydrous magnesium sulfate. Evaporation of the solvent on a rotary evaporator left a small amount of light yellow oil which was chromatographed through alumina (Woelm, acid washed, column 15 mm. x 30 cm.) using hexane

as eluant for the remaining diethyl fumarate followed by ether. The first cuts to come through after the fumarate showed one spot only on thin layer chromatography (silica gel, ether as developing solvent). When these cuts were combined and the solvent evaporated, a clear oil remained which crystallized from ethanol-water, m.p. 85-88°. Recrystallization from ethanol-water gave 0.023 g. of white needle crystals, m.p. 88-89°. This material exhibited ultraviolet absorption maxima at 224 mμ (ε = 14,300) and 287 mμ (ε = 22,300) in methanol. Significant infrared absorptions are (KBr): 5.78, 5.84, 6.01, and 6.28 (microns).

Anal. Calcd. for $C_{21}H_{26}N_2O_5$: C, 65.29, H, 6.74; N, 7.25. Found: C, 65.07, H, 6.64, N, 7.06.

CHAPTER V

SUMMARY

The mechanism of the thermal decomposition of N-nitroso-N-(2,2-diphenylcyclopropyl)ureas in non-polar solvents has been investigated. A mechanism postulating removal of a terminal $-NH_2$ proton by the nitroso oxygen atom through a cyclic transition state, followed by collapse to give isocyanic acid and the diazohydroxide is presented. Results reported earlier for the thermal decomposition of N-nitroso-N-methylurea substantiate this reaction scheme, and make it appear to be general for the thermal decomposition of alkyl nitrosoureas.

Heterically, the base induced conversion of N-nitrosoamides, urethanes and ureas to diazoalkanes has been postulated as proceeding via base attack on the carbonyl carbon to give a diazotate intermediate. However, results of a recent investigation excluded this path for the lithium ethoxide induced decomposition of N-nitroso-N-(2,2-diphenylcyclopropyl)ureas in non-polar solvents. Therefore, the mechanism of this decomposition was investigated more closely, and an alternate reaction scheme involving attack of the base on the nitroso nitrogen atom is postulated.

To generalize the results obtained in the study of the base decomposition of 5-nitroso-N-(2,2-diphenylcyclopropyl)urea, other derivatives of various N-nitroso-N-alkylamines were similarly investigated. Competitive attack of the base on the carbonyl carbon and the nitroso nitrogen atoms was found, with the relative amounts of each being highly dependent upon the conditions of the reaction. The manner in which a change in the solvent, the base or the alkyl substituent affects the mode of reaction of these nitrosoalkylamine derivatives is discussed. Information concerning conditions for preparing diazoalkanes in the highest yields is also given.

LIST OF REFERENCES

1. a. A. R. Huisgen and R. Reimlinger, Ann., 599, 183 (1956).

   b. A. Streitwieser, Jr., and W. D. Schaeffer, J. Am. Chem. Soc., 79, 2893(1957).

   c. E. B. White and C. A. Aufdermarsh, Jr., Ibid., 83, 1174, 1179(1961).

2. E. A. Werner, J. Chem. Soc., 115, 1093(1919).

3. K. Clusius and F. Endtinger, Helv. Chim. Acta, 43, 2063(1960).

4. W. M. Jones, M. H. Grosley and D. G. Ssarda, J. Am. Chem. Soc., 86, 912(1964).

5. K. H. Slotta and H. Tschesche, Ber., 60B, 295(1927).

6. I. Heilbron, "Dictionary of Organic Compounds," Vol. 1, Oxford University Press, New York, 1953.

7. C. Faurholt, J. chim. phys., 22, 1(1925).

8. T. K. Tandy, Jr., Ph.D. Dissertation, University of Florida, December, 1964.

9. H. von Pechmann, Ber., 27, 1888(1894).

10. A. Bantzsch and M. Lehmann, Ber., 35, 897(1902).

11. R. Huisgen and J. Reinertshofer, Ann., 575, 174(1952).

12. J. Tempe, H. Beslet and J. Morel, Compt. Rend., 258, 5420(1964); R. Huisgen, Ann., 573, 173(1951). C. D. Gutsche and L.K.C. Tao, J. Org. Chem., 28, 883(1963). See also C. D. Gutsche, Organic Reactions, Vol. VIII, John Wiley & Sons, Inc., New York, N.Y., 1954, pp. 389-390.

13. C. D. Gutsche and N. H. Johnson, J. Am. Chem. Soc., 77, 109(1955).

14. D. E. Applequist and D. E. McGreer, J. Am. Chem. Soc., 82, 1965(1960).

15. F. W. Bollinger, F. N. Hayes and S. Siegel, ibid., 72, 5592(1950).

16. B. R. Garrett, S. Goto and J. F. Stubbins, J. Pharm. Sci., 54, 119(1965).

17. H. Zollinger. Diezo and Azo Chemistry, Aliphatic and Aromatic Compounds. Interscience Publishers, Inc., New York, N.Y., 1961.

18. F. W. Bollinger, F. N. Hayes and S. Siegel, J. Am. Chem. Soc., 75, 1729(1953).

19. H. J. Becker and T. J. de Boer, Proc. Koninkl. Nederland Akad. Wetanschap 54B, 191(1951).

20. E. H. White, J. Am. Chem. Soc., 77, 6008(1955).

21. V. F. Gel'mov, J. Gen. Chem., U.S.S.R., 5, 1562(1935).

22. H. Heyns and A. Heins, Ann., 604, 133(1957).

23. O. Fischer, Ber., 28, 434(1895).

24. H. Amsel and A. W. Hofmann, Ber., 19, 1286(1886).

25. A. N. Kurtz and C. N. Niemann, J. Org. Chem., 26, 1843(1961).

26. J. L. Boivin and P. A. Boivin, Can. J. Chem., 29, 478(1951).

27. Organic Syntheses, Coll. Vol. II, John Wiley & Sons, Inc., New York, N.Y., 1943, p. 166.

28. J. W. Boehmer, Rec. trav. chim., 52, 379(1936).

29. J. S. Blair, J. Am. Chem. Soc., 48, 96(1926).

30. M. A. Bernard, Ann. de Chim. (Paris), 6, 81(1961).

31. T. L. Brown, D. W. Dickerhoof and D. A. Bafus, J. Am. Chem. Soc., 84, 1371(1962).

Cf. W. M. Jones, M. B. Gresley and W. S. Brey, Jr., J. Am. Chem. Soc., 85, 2754(1963) and references cited therein.

32. C. N. R. Rao, Collection Indian Inst. Sci. (Bangalore), Aug., 1961.

33. V. W. Reppe et al., Ann., 596, 150(1955).

34. B. Allen, Organic Syntheses, Vol. 12, John Wiley & Sons, Inc., New York, N. Y., 1932, p. 16.

BIOGRAPHICAL SKETCH

Darrel Lee Muck was born January 26, 1938, at Larned, Kansas. He graduated from Wichita High School East in Wichita, Kansas in May, 1955. The following September he entered the University of Wichita (Kansas) where he received the degree of Bachelor of Science in June, 1959, and the degree of Master of Science in June, 1962. He then continued his education by entering the Graduate School of the University of Florida in September, 1962. During graduate study he held both graduate teaching and research assistantships in the Department of Chemistry.

Darrel Lee Muck is married to the former Judith Ann Meyer and is the father of one child. He is a member of the American Chemical Society.

This dissertation was prepared under the direction of the chairman of the candidate's supervisory committee and has been approved by all members of that committee. It was submitted to the Dean of the College of Arts and Sciences and to the Graduate Council, and was approved as partial fulfillment of the requirements for the degree of Doctor of Philosophy.

August 14, 1965

Dean, College of Arts and Sciences

Dean, Graduate School

Supervisory Committee:

Chairman